MENDELIAN FACTOR DIFFERENCES VERSUS REACTION SYSTEM CONTRASTS IN HEREDITY[1]

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During recent years there has been a remarkable advance in our knowledge of Mendelian principles of heredity. This advance has for the most part had its source in the important and fundamental work of Morgan and his associates (1915) in which they have been concerned with the mutations of the common fruit fly, *Drosophila ampelophila*. The results of other work, in so far as agreement has permitted, have been brought into harmony with the principles arrived at through these investigations. As a result there has been developed a fairly clear and comprehensive conception of the constitution of the hereditary material and the nature of the mechanism by which it is distributed in gametogenesis, a conception which furnishes a consistent explanation of the products of Mendelian studies.

Morgan has stated that the fundamental principle of Mendelism may be reduced to this, that the units contributed by two parents separate in the germ cells of the offspring without having had any effect on each other. This conception of the absence of any factorial variability save that concerned in the discontinuous changes in factors involved in mutations has furnished the working hypothesis for Morgan's brilliant analysis of the germ plasm of *Drosophila*. Although the results of the *Drosophila* investigations have been ably presented elsewhere (Morgan et al., *l. c.*) it seems well briefly to review them here especially as they are vital to the argument presented in this paper.

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The large amount of data which Morgan and his associates have collected within the past six years has clearly demonstrated that the chromosome mechanism furnishes a basis upon which the behavior of Mendelian units may be logically and consistently explained. In an investigation of *Drosophila* over a hundred factor mutations have been discovered and studied, and these have been found to fall into four groups with respect to the linkage relations they display with one another. These four groups correspond to the four pairs of chromosomes. By determining the linkage values which are displayed within groups it has been possible to demonstrate that there is a consistent, invariable, linear arrangement of factors within the chromosomes at some time in their history. From this data Morgan and his associates have been able to prepare a map of the relative positions of the factors in the chromosomes. The complete conception, therefore, pictures the chromosome at some stage in its history as a linear series of loci. When a change occurs in some locus, a corresponding change of some sort may occur in somatogenesis, so that the individual which develops from such a set of factors with the changed locus differs in some particular way from an individual which develops from the normal unchanged series of loci. The change in the characters of the individual will depend not only upon the particular locus which has been changed, but also upon the particular way in which that locus has been changed. A changed locus, however, maintains the same position with reference to the other loci as did the unchanged locus, and this fact is the basis of Mendelian behavior, for knowing the behavior of the chromosomes in reduction, it enables us to gain a clear conception of the nature of Mendelian segregation.

When now we consider the particular factors themselves, the changed loci of the system, we see clearly that important physiological relations exist among the various loci. It is an appreciation of this fact that has led many investigators, among them Conklin (1908), Jennings (1914), Morgan (1915 *b*), Pearl (1915), and Wilson (1914),

to insist that the factors can not be regarded as determiners in themselves; but rather that they are differentiators, that working together with other factors in the system a difference is produced in somatogenesis which has its origin in some difference, some change in a locus in the system. For when in *Drosophila* a change in the locus *W* is produced, or in *Y*, such that the individuals developing from systems with these changed loci are white-eyed in the one case and yellow-bodied in the other, it seems evident that the change is more profound than the color of eyes or of body; that beyond these changes there is an underlying, elusive, physiological change resulting in individuals that are less vigorous and less fertile than those which develop from the normal unchanged system. The fact that a factor may have a primary, simple, easily recognizable effect and secondary far reaching effects, the latter to be attributed to the modified physiological relations resulting from a change in one of the members of a system, is one which has often been observed and which is of fundamental significance in our conception of the interrelations of the genetic factors. There are, however, other instances which may be cited of a somewhat similar nature, locus changes which produce certain characteristic effects under particular environmental conditions, but fail to disturb the normal behavior of the factor system when these conditions are not met.

It would, of course, be possible to recount almost indefinitely the specific effects of particular locus changes, whereas evidence concerning these far reaching effects of single factors is too scanty to warrant further discussion of this point. However, Morgan (1915 *a*) has been able to establish the relations displayed by the factor for abnormal abdomen and to demonstrate that only under very particular conditions is the presence of this genetic factor manifested by its characteristic expression, and that when these conditions are not present the product of somatogenesis may not differ in appearance from the normal fly, although differing from it both in genetic constitution and

hereditary behavior. We have thus a factor here which evidently has such a relation to the other members of the factor system that only under peculiar environmental conditions does it disturb the normal course of somatogenesis. Miles (1915) has likewise investigated a type of chlorophyll reduction in maize in which the recessive forms are yellow seedlings which usually show a distinct greenish tinge at the tips of the leaves. This type of chlorophyll reduction displays normal Mendelian behavior in inheritance giving in the progeny of heterozygous plants a ratio of approximately three seedlings which are of the normal green coloration to one which is of the yellowish type. The heterozygous plants possess the normal depth of coloration and can not be distinguished from those which are homozygous for the production of normal chlorophyll coloration. The yellow seedlings on the other hand form a distinct and easily recognizable class with no tendency toward intergradation, an observation which we have ourselves been able to confirm in independent mutations involving this locus. Usually these seedlings die as soon as the food material in the endosperm is exhausted, for under ordinary conditions the change in the locus is incompatible with a normal development of the individual, it is too profound an alteration to give a normally functioning factorial system. Miles found, however, that when the yellow seedlings were grown under particularly favorable conditions, they developed a normal chlorophyll coloration and produced plants which were able to go on through the cycle of changes included in the normal development of the maize plant. Now this behavior can not be referred to any change of the reduction locus back to the original condition, for the progeny of such plants consisted entirely of yellow seedlings; indeed, such a reversion would be inconceivable. Obviously the explanation of the situation will be found only through a consideration of the system with the recessive reduction locus. Normally this unchanged locus performs a definite function in determining the production of chlorophyll in the plant, but this function is

performed in conjunction with a number, perhaps a very great number or even all, of the other loci within the system. With a change in this particular locus, however, comes a change in the normal course of events in chlorophyll production, in that the rate at which the system is able to produce chlorophyll has been altered. Nevertheless, this change does not completely prevent the system under favorable conditions from going on and ultimately developing the same reaction end product which would have developed in the normal unchanged condition, but more rapidly.

Among such factors as have a profound influence upon the interrelations within the systems of which they are a part are those which Morgan (1914) has called lethals. Morgan's work with lethals is particularly suggestive because he has been able to demonstrate that they, like other normal Mendelian factors, occupy a definite locus in the chromatin system and display the same perfectly definite and consistent behavior with reference to the other loci of the system as do all other changed loci which do not interfere with the normal development of the individual. It is entirely possible that some of the lethals, like the chlorophyll reduction locus which we have discussed above, may yield systems which occasionally permit of the normal development of the individual, at least certain peculiar sex ratios which have been obtained might indicate that fact (Morgan, *l. c.*); but the important result of these investigations with lethal factors lies in that fact that certain kinds of changes in some loci are incompatible with normal functioning of the chromatin system. It might in addition be noted that there seems to be no particular reason why we should not include in the same category with lethals, the type of chlorophyll reduction mentioned above and those other types in maize which result from such profound factor changes that no development is possible after the food supply of the endosperm is exhausted.

Now giving the above results their broader and more general interpretation, it would appear that the factors

make up a reaction system the elements of which bear a more or less specific relationship to one another. It is this specific interrelation of the factors of the reaction system which determines that wheat produces wheat, and corn, corn, and so on through the whole realm of living matter. With this in mind it is at once apparent that normal Mendelian behavior can not be considered as a contrast of different reaction systems, but that in such cases the two organisms contrasted must possess fundamentally the same reaction systems, only a relatively few elements within the reaction system differing, and these not in a fundamental fashion. In fact it seems entirely logical in the light of modern Mendelian developments to consider each particular locus as made up of a definite nucleus, some complex organic compound perhaps, with a number of end chains which may be altered in various ways without changing the structure of the nucleus of the locus. According to this conception the fundamental relation of the locus to the other elements of the reaction system would remain unchanged, while the end product would be altered in some particular manner. There is probably no more striking confirmation of this conception than the suggestive hypothesis of multiple allelomorphs which Morgan and his associates (1915, *l. c.*) have developed. Their results and those of others in this connection seem to show clearly that the explanation of Mendelian differences on the basis of such a profound change as the dropping out of an element from a delicately balanced reaction system is practically out of the question. In multiple allelomorphs we have not one, but several, changes within the same locus. The similar effect which these changes have on certain organs of the body, for example, that relation shown in the locus *W* in *Drosophila* as a consequence of which the normal red eye color may be changed to white, eosin, or cherry depending upon a particular change in the locus, are such as to indicate that these are probably changes around the fringe of the molecule and not such as fundamentally affect the structure of the entire locus. Moreover, the relations thus exhibited again indicate that

the locus has a particular place and function in the reaction system, that it bears a specific relation to the other elements of the system.

It is true that investigation in plant breeding has not yet progressed far enough to furnish a definite confirmation all along the line of the work with *Drosophila.* The reasons for this are very obvious and they lie in the technical difficulties involved in such work rather than in fundamental disagreements in principle. It has not as yet been possible to study as many factors in any plant species as have been investigated in *Drosophila,* nor to carry the work through as many generations nor to employ as large populations. Moreover, most plant material is more difficult to handle from the standpoint of a chromosome analysis on account of the longer period of time necessary to secure data and the greater amount of attention which must be given the cultures and the larger number of chromosomes which are usually involved in such species. It must also be borne in mind that practically all the *Drosophila* differences have arisen under observation as simple factor mutations, and it has therefore been relatively easy to determine their relations to the other factors in the system. In plants, on the other hand, the material has presented itself as a confusing array of varieties containing for the most part a large number of recessive factors, and usually the original form from which they were derived, corresponding to the *normal* fly of Morgan's work, has not been obtainable and would not have been particularly useful, had it been available. Nevertheless, there appears to be no real difficulty in the way of accepting the conception derived from the *Drosophila* studies as a definite, consistent working hypothesis; for it is difficult to believe that the behavior of plant material should be fundamentally different, and indeed points of correspondence are not lacking to warrant us in viewing somewhat sceptically any undue emphasis placed upon the differences which may seem to obtain.

We may now return to the conception of the reaction system as a unit in itself in the sense that it is made up of

a large number of elements which bear a more or less specific relation to one another. This is the important physiological conception which has grown out of the vast amount of work which has been done in recent years in the analysis of the hereditary material. This is no new contention; it has been advanced and ably advocated by many investigators, but we feel that certain consequences of this conception have not been given the consideration their importance deserves. For if this conception be valid then it should not be possible, in certain cases at least, to shift and recombine the elements from which systems have been built up in the haphazard way that some advocates of Mendelism have attempted to do. If, for example, it is possible to obtain hybrids involving not a contrast between factors within a single system, but a contrast of systems all along the line, then it is obvious that we must consider the phenomenon on a higher plane, we must lift our point of consideration as it were from the units of the system to the systems as units in themselves.

Our attention has been called to this extension of the Mendelian conception by the behavior of species hybrids of *Nicotiana* which have been studied at the University of California during the past six years. This study has been concerned particularly with hybrids between *N. sylvestris* and varieties of *N. Tabacum*. These species, the former represented in the collections of the University of California Botanical Garden by a single type and the latter by a considerable variety of distinct forms, belong to entirely distinct sections of the genus *Nicotiana* and differ in important particulars which have been described elsewhere (Setchell, 1912). Goodspeed (1913) has studied a large number of different reciprocal hybrids between *sylvestris* and various of the distinct varieties of *Tabacum*. These hybrids are all partially sterile. It is possible to obtain a few viable seeds from open pollinated flowers and from those pollinated with *Tabacum* and *sylvestris*, but it has never been found possible to obtain any selfed seed. The phenomena displayed by these hybrids in development and inheritance admit of a consistent ex-

planation, if we regard them as the outcome of a contrast of two distinct Mendelian reaction systems the elements of which can not be freely interchanged without profoundly affecting the general functions of the reaction systems thereby resulting. We shall take up in very general fashion the points which have inclined us to this view, reserving for a later treatment the discussion of the hypothesis in detail and also the presentation of the extended data.

When hybrids are obtained between *sylvestris* and the various varieties of *Tabacum* they agree throughout in F_1 in presenting the entire set of characters of the *Tabacum* parent to the exclusion of those of *sylvestris*. This behavior may be definitely accounted for as a dominance of the *Tabacum* reaction system as such over the *sylvestris* reaction system. For point by point and character by character throughout, the correspondence between the *Tabacum* variety and its F_1 *sylvestris* hybrid may be demonstrated in a remarkable fashion and this irrespective of whether the factors concerned in these character expressions in the *Tabacum* varieties are dominant or recessive in varietal crosses. This correspondence is not only apparent in general appearance, but it extends to minute details of form and structure, and it is displayed even in the more intangible characteristics generally included under the term habit—*i. e.*, such characteristic varietal peculiarities of expression as the method of branching, insertion and inclination of the leaves, the type of inflorescence, and so on through a whole series of details. For example, when *N. Tabacum* var *macrophylla* (Setchell, *l. c.*, p. 8) is the *Tabacum* parent, the F_1 hybrids display the particular appearance and also the particular characteristics of *macrophylla*, except that throughout they are expressed on a very much enlarged scale (*cf.* East and Hayes, 1912). The broad clasping leaf of *macrophylla* with its distinctly pointed tip is faithfully reproduced in the hybrids. The flowers show no effect of the very much elongated corolla tube and the lobing of the limb peculiar to *sylvestris*, but display the *macrophylla*

proportions throughout. The stout tube, swollen infundibulum, and pentagonal limb are clearly derived from *macrophylla,* and the color is rose red of approximately the same depth and tone as that of *macrophylla* and in striking contrast to the pure white of *sylvestris.* In habit the hybrids resemble *macrophylla.* In early growth they are not characterized by the long maintained rosette which is so characteristic of *sylvestris,* and in leaf distribution, branching, and type of inflorescence they again correspond to their *macrophylla* parent.

When an entirely different set of characters is concerned in the *Tabacum* parent the F_1 hybrid with *sylvestris* is still an exact replica of the particular *Tabacum* used. For instance *N. angustifolia* (Setchell, *l. c.*, p. 9) and *sylvestris* give a hybrid which is entirely different in general appearance and all details from that obtained between *macrophylla* and *sylvestris,* and which displays throughout the *angustifolia* characters. The leaves of the hybrid are obliquely ovate-lanceolate and taper gradually to a long, curved point. They are also distinctly petioled like those of *angustifolia.* These characters are in striking contrast to those characteristic of the leaves of *sylvestris,* which are broad throughout, broadly pointed, and have a broad clasping base. When flower characters are examined, *angustifolia* is again faithfully reproduced in the F_1 hybrid for its flowers have the slender, straight corolla tube with practically no suggestion of an infundibulum and the deeply divided limb with narrow lobes that taper into long slender tips, all so characteristic of *angustifolia.* Like those of *angustifolia* the flowers are pink. In habit these hybrids again resemble *angustifolia.* This resemblance is displayed in a particularly striking fashion in the graceful, drooping manner in which the leaves are borne in marked contrast to the stiff, erect manner in which the leaves are borne by *sylvestris.* Throughout, *macrophylla* and *angustifolia* present a strikingly contrasted set of characters, yet in each case they are reproduced in their entirety in F_1 of the hybrid with *sylvestris.*

When particular tagged Mendelian factors are considered the same behavior is displayed. Perhaps there is no more striking instance of this than that shown by the expression of the calycine flower type in these *sylvestris* hybrids. When *N. Tabacum* var. *calycina* (Setchell, *l. c.*, p. 6) with its peculiar split, hose-in-hose flowers is crossed with *Tabacum* varieties of the normal flower type, the F_1 hybrids display the normal flower form and segregation occurs in F_2 into normal and calycine in accordance with simple Mendelian expectations. But when the *Tabacum* reaction system carries the recessive calycine flower factor into these species hybrids with *sylvestris* then every flower on the F_1 plants displays a more or less calycine structure. Similarly when the parthenocarpic characteristics of *N. Tabacum* var. "Cuba" (Goodspeed, 1915) are carried in by the *Tabacum* parent then the F_1 hybrid, instead of shedding its capsules soon after anthesis as is the case in all the other *Tabacum-sylvestris* hybrids, retains them indefinitely, in spite of the fact that no good pollen is produced, and thus non-fertilization, the stimulus for fruit abscission in *Nicotiana,* here also is the rule. So far as present evidence indicates this characteristic is rather strictly confined in *Nicotiana* to the variety "Cuba." This behavior of recessive factors of *Tabacum* varieties in hybrids with *sylvestris* is a striking confirmation of the conception that in such cases there is a contrast between distinct reaction systems rather than between certain factors as opposed to each other. In general when *Tabacum* varieties of the type mentioned above are crossed with each other the hybrids, especially with respect to flower color, leaf shape, etc., are intermediate. The contrast in this case is not one between two distinct Mendelian reaction systems, but it is merely a contrast of certain differences within a common system, and the segregation in subsequent generations, although complex, indicates a general accordance with normal Mendelian expectation. But in the case of species hybrids between *Tabacum* and *sylvestris* the contrast is between distinct

Mendelian reaction systems and the consistent reproduction of all *Tabacum* characters, whether qualitative or quantitative, indicates at one and the same time that these are fundamentally of the same nature, depending essentially for their expression on a complex set of Mendelian factors, and, moreover, that the *Tabacum* system as a unit dominates the course of somatogenesis and determines the reaction end products of the two systems.

This domination of the somatogenic processes by the *Tabacum* reaction system is followed by important experimental possibilities. If the species hybrids always display the *Tabacum* characteristics as completely as all our present evidence indicates that they do, then they will furnish a powerful method of attack on the problem of Mendelian behavior in the *Tabacum* section of the genus *Nicotiana*. For by crossing hybrids between *Tabacum* varieties with *sylvestris,* it should be possible to secure in the partially sterile hybrids resulting a phenotypic reproduction of the gametic series of the *Tabacum* parent. This series would not be complicated by intergrading of heterozygous forms, because the plants thus obtained would exhibit the phenotypic characters of homozygotes, and recessive factors as well as dominant ones would be reproduced in their proper place in the *Tabacum* system. Apparently it should be possible, therefore, to demonstrate the fundamentally similar nature of linkage in *Nicotiana* and *Drosophila*. Such an analysis will still be very difficult in *Nicotiana* on account of its high chromosome number, but by the method of procedure outlined above some distinct advance at least seems perfectly feasible. These, however, are matters on which we have as yet very little data.

Since, therefore, the *Tabacum* reaction system dominates the somatogenic processes in the hybrid to nearly or quite the exclusion of the *sylvestris* system, the elements of the two systems must be largely mutually incompatible. Free interchanges between the two systems would not, therefore, necessarily result in the formation

of functional Mendelian reaction systems. This high degree of mutual incompatibility of the two reaction systems exhibits itself in the high degree of sterility of the F_1 hybrids. As Goodspeed (1912, *l. c.*) has shown, however, this sterility is only partial and a few good ovules are formed which produce viable seed in the case of open pollination or when crossed back with the parents. In evidence which is presented elsewhere (Goodspeed and Ayres, 1916) it has been shown that, while it is experimentally possible to modify the behavior of the F_1 plants in such a manner that the fruits without pollination are retained for a considerable period rather than falling soon after anthesis, the percentage of good ovules produced can not be appreciably modified. This is an important point, for it indicates that the number of good ovules produced is a function of the chromatin behavior and not to be influenced by environmental factors, and that they should, therefore, exhibit a consistent behavior and lend themselves to a logical interpretation. In fact, evidence at hand indicates that the small percentage of functional ovules represents the *Tabacum* and *sylvestris* extremes of a recombination series, and that, therefore, the middle members of the series, which are made up of relatively high proportions of both *Tabacum* and *sylvestris* elements, fail to function because they produce incompatible reaction systems. This is shown clearly by back crosses which have been made with the parents, although here portions of our evidence are not so well controlled as we would prefer. When back crosses are made with *sylvestris* as the pollen parent there is produced a variety of forms many of which are highly abnormal, but among them there is a considerable proportion of plants which are pure *sylvestris* in all characters. These plants are fertile and have bred true to the *sylvestris* type for three generations. A number of the remaining plants resemble *sylvestris,* but show contamination with other elements presumably derived from the *Taba-*

cum reaction system. These contaminations affect the whole plant, not alone any particular character complex. All plants except those which were of the pure *sylvestris* type were sterile. Until this year we have not been able to secure seed from back crosses with the *Tabacum* parent, but from open pollinated seed a variety of forms is produced, practically all of which are of the *Tabacum* type in general appearance. This result is evidently due to pollination of the F_1 flowers with pollen from the wide series of *Tabacum* forms which, in predominating numbers, have always been grown in the cultures. Some of these plants resulting from uncontrolled pollination were likewise fertile. They have been grown for several generations and although displaying segregation, this segregation has never involved the production of *sylvestris* characters, but has been of a type normally found within varietal hybrids of *Tabacum*. The sterile forms in this series largely resembled the F_1 hybrids of *Tabacum* and *sylvestris*, and the occurrence of a few aberrant and *sylvestris* forms which were obtained from the sowing of the open pollinated seed are what would be expected, if pollination was sometimes effected with *sylvestris* pollen.

It appears, therefore, that for these species hybrids the conception of the factors as making up for each species a reaction system in which the elements have a specific relation to one another harmonizes the results obtained with the more recent Mendelian developments. The objection which might be made that interchanges of factors which behave normally in one system should not logically be followed by such profound disturbances as to completely prevent the formation of a functional reaction system is met by several counter considerations. In the discussion of lethal factors it has been pointed out that Morgan (1914, *l. c.*) has demonstrated that changes in many loci of the *Drosophila* system have been followed by failure of the resulting individual to develop. It is entirely conceivable that, if a certain factor *A* in one system

be considered, the corresponding factor A' in the other system, if there be such a factor, might be just as different from A as a lethal factor is different from its normal allelomorph. Further, from a modern Mendelian viewpoint there is no basis for assuming that recombinations could be obtained involving only exchanges in isolated loci in the systems. For if the behavior in segregation in the F_1 hybrids corresponds to that in *Drosophila* then such combinations as could be obtained would depend on the shifting of entire choromosomes or in case of crossing-over of relatively large portions of chromosomes. The recombinations obtained in the hybrids between *Tabacum* varieties and *sylvestris,* provided chromosome distribution takes place after the normal fashion in these hybrids, would involve, therefore, for the most part, the formation of systems containing either whole chromosomes or large sections of chromosomes of opposing systems. Such attempted reconstruction of systems might well fail in cases of any marked specificity in the relations of the factors of the opposing reaction systêms, since any large proportions of both systems in a gamete might conceivably destroy the continuity or the balanced relations necessary for the continuance of system reactions. When the proportions of one or the other system are relatively small, the system reactions might be merely disturbed, resulting in the production of the abnormal forms which have been secured in our cultures. It is to such relations between the two systems involved that we ascribe the selective elimination of the greater portion of the possible gametic combinations in the crosses between *Tabacum* varieties and *sylvestris,* and which, therefore, results in a high degree of sterility in these hybrids.

It is of course obvious that there are many categories of sterility, in the hereditary sense as well as in the physiological sense. The particular type herein considered is that which results from relatively wide crossing such as is involved in species hybrids. That certain types of steril-

ity are due to specific factors which display consistent Mendelian behavior has been demonstrated by Bateson and Punnett (1908) and others and has been suggested by Correns (1913) for cases which are concerned with the specific category of normal self-sterility in *Cardamine pratensis*. It appears, nevertheless, as East (1915) in principle has suggested, that many cases in which sterility has followed rather wide crossing would seem to be susceptible of a more logical treatment from the standpoint of non-specific disturbances in the reaction systems involved.

(*To be continued*)